Remarks

The July 1, 2003 Official Action has been carefully reviewed. In view of the amendments submitted herewith and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

In the Official Action, the Examiner has rejected claims 1, 4, 5, 8-10, 18-20, and 73 under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable a skilled artisan to make and/or use the invention.

The foregoing rejection constitutes all of the grounds set forth in the July 1, 2003 Official Action for refusing the present application.

Claims 1 and 18 have been amended to more particularly point out and distinctly claim the invention. Specifically, the amendments are those proposed in the May 19, 2003 correspondence to the Examiner to clarify the perceived ambiguity with the molecular modeling step. No new matter has been introduced into this application by reason of these amendments.

CLAIMS 1, 4, 5, 8-10, 18-20, AND 73 FULLY COMPLY WITH THE REQUIREMENTS OF 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 1, 4, 5, 8-10, 18-20, and 73 under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. The Examiner alleges that the specification does not describe the dynamic filtering process in sufficient detail to allow a skilled artisan to practice the claimed invention without undue experimentation.

Applicants submit that the Examiner is correct in recognizing that Applicants' specification specifically discloses that the dynamic filtering process can be performed using the Multidyn software as described at page 17, lines 19 to 24. However, Applicants point out that this reference at

page 17 is only one of several references to such a filtering process in the application. Indeed, the derivation and use of dynamic filters is also described in broad terms from page 9, line 3 to page 10, line 10. The dynamic filtering process is also described in very detailed terms from page 35, line 3 to page 37, line 23. Applicants note that this detailed description section is similar to the description presented in the inventors' paper published in Nature Biotechnology (Grassy G. et al. (1998) 16:748-752), a journal well known for its high standards of scientific quality and accuracy.

Applicants submit that the Multidyn software is merely a convenient platform which allows the user to avoid the file reformatting which would otherwise be required when transferring data between other commercial software. In order to achieve dynamic filtering without using the Multidyn software, the skilled person could perform the steps at page 35, line 3 to page 37, line 23 which describe how "the peptides were investigated from the aspect of their conformational spaces (dynamic filter)" (page 35, lines 6 to 7). The steps of the dynamic filtering process are as follows.

The first step is described from page 35, line 10 to page 36, line 5. Briefly, the initial data needed to compute the dynamic filter can be obtained by generating a molecular dynamics trajectory for each molecule of interest, under conditions which seem appropriate to a person skilled in the art. This can be achieved by using any commercially available molecular dynamics software such as, for example, AMBER (University of California San Francisco, USA; see Applicants' specification at page 35, lines 12 to 14) or Insight (Accelrys Inc, San Diego, USA). As indicated at page 36, lines 2 to 5 and in the following step, each conformation extracted from the trajectory is then used to calculate its 3D autocorrelation vector (3D-ACV).

The second step of the dynamic filtering process,

which entails calculating 3D-ACVs, is described from page 36, line 2 to page 36, line 25. The 3D-ACV of a given conformation can be calculated by using the TSAR software (Accelrys Inc, San Diego, USA; see Applicants' specification at page 30, line 30). Alternatively, the calculation of a 3D-ACV is straightforward to program for a person skilled in the art. As described in detail at page 36, lines 11 to 25 and in the European Journal of Medicinal Chemistry article referenced on page 36, lines 4 to 5 of Applicants' specification, the process consists of the calculation, for a given conformation of a given molecule, of all the interatomic distances for each pair of atoms of the molecule. The 3D-ACV is the histogram of all the interatomic distances using a given step (e.g., a step of 1 angstrom).

The final step of the dynamic filtering process is described from page 36, line 26 to page 37, line 18. As noted at page 36, line 26 to page 37, line 3, the 3D-ACVs of all the extracted conformations of a molecule are together called a "multiple 3D-ACV." In other words, the 3D-ACVs together represent all the conformations of a given molecule. In order to compare the multiple 3D-ACVs of all the molecules of interest, each of them is transformed by calculating their corresponding principal components (see page 37, lines 4 to 11 of Applicants' specification). This is achieved by using a Principal Component Analysis (PCA) calculation, which is a standard data reduction technique which can easily be found in most commercial statistical packages like TSAR (Accelrys Inc, San Diego, USA), Statistica (Statsoft, Tulsa, USA), or SIMCA (Umetrics, Umea, Sweden) amongst many others. Such programs are also readily obtained as freeware versions from the internet. Each 3D-ACV is reduced to a dot in the plane made by the 2 first component axes. Hence, each multiple 3D-ACV becomes a set of dots directly related to what is called "the conformational space" (see page 37, lines 11 to 14 of Applicants' specification). The conformational spaces of the

molecules of interest, i.e. the corresponding distributions dot clusters, are then compared in terms of overlapping or similarity, as described at page 37, lines 4 to 16. The above analysis can be performed using the Multidyn software as mentioned at page 37, lines 16 to 18, but Applicants submit that the skilled person would know that any other standard cluster analysis technique or software package could be used.

As noted at page 37, lines 19 to 23 of Applicants' specification, the dynamic filtering identified one of the five peptides (RDP1277) selected by the static filters as having a conformational space very different from the other four peptides. This one peptide was biologically inactive, whereas the other four peptides were active in the graft survival assay. This demonstrates the effectiveness of the dynamic filtering process.

In view of the substantial contribution to the art made by the present invention and the detailed description of the dynamic filtering process which relieves the skilled person of having to perform undue experimentation, the breadth of the claims are entirely justified. Therefore, Applicants respectfully submit that the rejection of claims 1, 4, 5, 8-10, 18-20, and 73 under 35 U.S.C. §112, first paragraph is without merit and respectfully request its withdrawal.

CONCLUSION

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the rejections set forth in the July 1, 2003 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issue may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

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